

B Scene



Vol 1, No. 1 • Bioscience Division Newsletter • January 17, 2000

Welcome to **B Scene**

Bioscience Division welcomes you to the first issue of **B Scene**. Our bi-weekly newsletter has been developed to build and enhance communication within the division. The newsletter will include contributed articles and information about activities, issues, and events. It is our newsletter- so, please read and enjoy!

Please send all news items, comments, and suggestions for future issues to:

bscene@telomere.lanl.gov

Look for:

- *B Division news*
Including "From Jill's Desk"
- *Bravo*
Awards and accomplishments
- *Breaking News*
Publications and laboratory successes
- *Bucks*
Program opportunities and reports
- *B Heard*
Letters and comments
- *B There*
Calendar of events and meetings
- *B Serious!*
Humor

Meet the Resource Managers



Left to right: Robert Atcher (B-S1), Basil Swanson (B-N2), Jill Trehwella, Jim Brainard (B-N1), and Paul Gilna (B-S2).
Photo by Liz Padilla, Public Affairs Office.

Bob Atcher joined the Nuclear and Radiochemistry Group at Los Alamos in 1997 after a full research career in medicine. After receiving his PhD from the University of Rochester in nuclear chemistry, he was a research fellow in radiology at Brigham & Women's Hospital and Harvard Medical School. He then worked in the Radiation Oncology branch at the National Cancer Institute before moving to Argonne National Laboratory in 1986, where he enjoyed a dual appointment as Assistant Professor of Radiation Oncology at the University of Chicago until 1994. Moving to the University of Alabama in 1994, he worked as Associate Professor of Radiation Oncology prior to joining LANL. He currently has an appointment as Clinical Professor of

Pharmacy with the University of New Mexico. Bob sits on several review committees for the National Institutes of Health, using his expertise in the use of radioisotopes for therapy and imaging. Some of his major research interests include use of radiolabeled biomolecules for diagnosis and therapy, short-lived radionuclide generator products for use in medicine and basic studies in radiochemistry and nuclear chemistry. He is married to Sharon Atcher who is group office administrator in CST-11 and has one son, Andrew (age 8), from a previous marriage who lives with his mother in Chicago. A professional musician during his undergraduate and graduate studies, he lists (not surprisingly) music as one of his hobbies, both playing

and listening. "I also enjoy theater though I have much more limited opportunities to see live theater than when I was in Chicago. Sharon and I took up golf this year as a way to spend some time outdoors. We have also diligently bought ski passes at Pajarito for the last two years and will take full blame for the lack of snow. We decided that having golf as an option if it was a dry winter was smart.... although we didn't count on a COLD dry winter."

Jim Brainard joined Los Alamos National Laboratory as a postdoctoral fellow following an NIH post-doc fellowship at Baylor College of Medicine. He received his Ph.D. from Indiana University in chemistry. He became a staff member in 1983 and worked in CST Division before becoming a Resource Manager for B Division this fall. His current research interests include biotransformations of xenobiotics by isolated enzymes, microorganisms and microbial communities, mediation of toxic and radioactive metal speciation, and environmental transport by microorganisms. He is currently principle investigator of an LDRD-DR, Bioremediation Science to Meet National Challenges. He is married to Debbie Ehler and is father of two sons: Bob lives in south bay area of California and Andy lives in Placitas. "My main hobbies are skiing and sailing, but just small boats...not big ones."

Paul Gilna joined the Theoretical Division at Los Alamos in 1988 following a research career at the University of Chicago where he published a number of heavily cited papers on cloning and expression of Human Steroid Receptor proteins. He joined the LANL GenBank international nucleotide sequence database project and was instrumental in establishing the National Center for Genome Resources, a not-for-profit bioinformatics company based in Santa Fe, NM. He also served as Program Manager for the DOE Office of Biological and Environmental Research-funded activities at LANL. For the past two years, Paul has been on Change of Station to the National Science Foundation based in Arlington, Virginia where he administers programs in bioinformatics and computational biology. He lists among his accomplishments there, stewardship of the successful transition of the Protein Structure Database (PDB) to a new home, development of a new research program focused on funding research in biological databases and informatics, and installation of the first all-electronic peer-review system at NSF. Paul, his wife Margot and their four children expect to return full-time to the Los Alamos environs at the beginning of the summer. Paul enjoys recreational activities, skiing and photography and has served as an officer and president of the Los Alamos Ski Racing Team.

Basil Swanson joined the Lab as a staff member in January of 1980 after serving as an Assistant Professor of Chemistry at the University of Texas at Austin. Four years later, he became group leader (INC-4) and led efforts to build and recruit staff, some of whom have now become leading scientists at the Laboratory. He was named a Laboratory Fellow in 1991 and in 1993 took a

two-year leave of absence from research to serve as the project Leader for Laboratory Strategic Planning during the time of the Galvin Commission Study. "My own research efforts have shifted in recent years to self-assembly, biomimetic materials and the development of advanced sensors based on lessons from nature. A promising example of cross-fertilization in the new Division is to couple molecular diversity research efforts with the design and preparation of recognition molecules for biosensor development." Swanson enjoys skiing and woodworking and frequently combines his photography hobby with motorcycling. He also takes credit for encouraging members of his family to study chemistry, citing a nephew at Stanford, a son at UC-Irving studying atmospheric science and a daughter at UC-Davis studying biochemistry.

➤ *Written by Sandra Zink.*

From Jill's Desk



I have greatly enjoyed these first few months of B Division – they have been fast paced and I am looking forward to some "normalization" over the next few months for us all. We have learned a great deal as we have developed new ideas and concepts of how we want to operate to achieve our technical vision. In describing to people what we have done, I have developed a deeper understanding of the potential we have. I am looking forward to be out in the different resource areas this month to tell you a little of what I have learned, what our new management model really is, and to listen to your issues.

One of the things I did just before the holidays was to call our nominated Division Review Committee members and ask them if they would be willing to do extra work for inadequate compensation! When I described our new organization, I was gratified to find enthusiastic responses. The Director is now following through with formal invitations and we are doing the paper work in time for our first DRC meeting May 25-26, 2000. The B Division Review Committee will include: Janet Dorigan, Senior Scientist in the Office of Research and Development of the Central Intelligence Agency; Walter M. Fitch, National Academy of Sciences (NAS), Professor of Ecology and Evolutionary Biology at UC Irvine; Art Friedlander, Senior Advisor U.S. Army

Medical Research Institute of Infectious Diseases; David Galas, Chief Academic Officer, Vice President and Professor at the Keck Graduate Institute; Raymond F. Gesteland, Professor of Biology and Chairman of Human Genetics at the University of Utah; Harry B. Gray, NAS, Professor of Chemistry Caltech; David S. Kliger, Dean of Natural Sciences UC Santa Cruz; John Bertram Little, James Stevens Simmons Professor of Radiobiology Harvard University; George Weinstock, Professor of Microbiology and Molecular Genetics University of Texas Medical School at Houston. We can all look forward to working with this very distinguished group as we move forward.

-Jill

Communications Team Report

The Communications Team is very active and has several new initiatives. *B Scene*, Bioscience Division's newsletter, with Babs Marrone as Editor, will be published every two weeks. A new B-Division web site is also in the works and will be coming on-line by Feb. 1st. Min Park and Tracy Ruscetti are heading up our science outreach activities and are looking for volunteers who will commit to lectures and visits to schools. If you are willing to help, please send a message to Min Park at park_min_s@lanl.gov with some indication of your availability and your area of expertise. Ternel Martinez in Public Affairs also sits on our Communications Team and will be working closely with us to produce articles and news releases about B Division accomplishments. He is also assisting us in the development of a communications plan for publicizing B Division success stories to our local community. Tamara Johnson is taking responsibility for working with our staff and the Bradbury Science museum to upgrade and improve our science exhibits. We also have a **Scrapbook!** Please bring news clippings, photos, anything that is of general interest to me and I will make sure they will be included in the Scrapbook. We will make the Scrapbook available in the library for all to browse through once the library renovations are complete. We want to make B Division a model division for managing communications effectively...both internal to the Division, internal and external to the Laboratory, and external to our local and regional communities, so let me hear from you about how we can do our job better (zink@lanl.gov).

➤ Contributed by Sandra Zink, Team Leader

Report from Facility Management

Facility- The office refurbishing project at HRL is underway. Last week cubes in 201, 107 and B225 were furnished with new desks. Due to a problem at Contract Associates, new chairs will be delayed several weeks. We will be offering instructions on how to adjust the computer tables, then we'll get the word on how to adjust the chairs. It is our goal to get ergo-furnishings for all workstations in labs and at other sites. Following this first phase we will assess what more is needed.

Safety- There are some new LIRs (Laboratory Implementation Requirements) that will be affecting work as we know it. The first is the Chemical Management LIR. Some of you are already getting electronic requests to account for chemicals in your inventory. In addition there are two LIRs that address "Authorization Basis" (how we determine what work we can do safely and where we can do it- or not do it, as the case may be). To help you understand what has to continue, or change, for us to be in compliance with these documents I will have a TECH TIME at HRL on Thursday 20 January and then I'll do the same presentation in the TA-35 conference room on February 2. We will also use this opportunity to do a little cultural exchange. Following my discussions of the LIRs, I will do a tour of TA-43-HRL labs, and someone familiar with -35 will provide a tour of the Biotech Facility at TA-35 on the 2nd of Feb. I encourage HRLers to go -35 for the tour and TA-35, -46ers to come to HRL. I will provide lunch-type munchies at both sites. In March we will do another TECH TIME in the TA-35 conference room, then tour TA-46 B-Division activities at the ISL.

➤ Contributed by Julie Wilson

B Serious!



Bucks

OBER Report

The following seven high quality preproposals have been submitted to OBER for review in response to their call entitled, "Experimental and Computation Structural Biology". Numerous folks from around B, T, STB, CST, and P contributed to different aspects of this effort and the result was a very strong response.

Bruno, B, "Relationship of Sequence to Structure and Function through Phylogenetic Analysis of Covariation and Adaptation in DNA Repair Proteins"

Chen, X. "Structural and Dynamical Analysis of a Multi-Protein DNA Damage/Repair Complex using Integrated Stable-Isotope Assisted (SIA) Mass Spectrometry, SIA/NMR, and Planning and Data Analysis Algorithms".

Donohoe, R., J. Brainard, S. Burde, D. Clark, D. B. Dyer, D. Morris, M. Neu, W. Woodruff, "Structural Dynamics of Metal Reducing Proteins in *Shewanella putrefaciens*".

Dyer, B., M. Park, "Real-time spectromicroscopic imaging of DNA damage recognition and repair".

Park, M., T. Terwilliger, J. Berendzen, G. Waldo, B. Brunno, "Large-scale Structure/Function Studies of DNA Repair Proteins from *Deinococcus radiodurans*".

Trehwella, J., C-S Tung, "A combined experimental and computational approach to structural studies of proteins involved in the repair of DNA damage due to ionizing radiation".

Unkefer, C., A. Garcia "Rational Engineering of Enzymes for Bioremediation: A Coupled Experimental and Computational Approach".

Three new funding opportunities are available:

1) Carbon Sequestration Research Program. From the Office of Biological and Environmental Research (OBER). Research on Carbon Sequestration in the Terrestrial Biosphere and the Oceans. Due date: March 2. More info at:
http://www.er.doe.gov/production/grants/fr00_09.html

2) Natural and Accelerated Bioremediation Research Program. From the Office of Biological and Environmental Research (OBER) of the Office of Science, U.S. Department of Energy (DOE). Research in the Natural and Accelerated Bioremediation Research (NABIR) Program. Proposals should describe research projects in one of the following categories:

1. Scientific aims of individual NABIR elements including Biogeochemistry, Biotransformation, Community Dynamics, Biomolecular Science and Engineering, and Assessment.

2. Research projects to be performed at a Field Research Center addressing field scale biostimulation of microbiological processes that immobilize metals and/or radionuclides.

Interdisciplinary teams should include experts in the fields of microbiology, geochemistry, and hydrology.

Due date: February 28. More info at:

http://www.er.doe.gov/production/grants/lab00_05.html

3) Biotechnological Investigations - Ocean Margins Program. From the Office of Biological and Environmental Research (OBER) of the Office of Science (SC), U.S. Department of Energy (DOE). Research involving the use of molecular biological and biogeochemical techniques to understand the linkages between carbon and nitrogen cycles (primary production and microbial processes) in ocean margins. Due date: February 10, 2000. More info at:

http://www.er.doe.gov/production/grants/lab00_04.html

➤ *Contributed by Scott Cram and Ed Hildebrand*

NIH Report

Jim Freyer writes: "I have been asked to author a regular feature in B Scene concerning all aspects of research funding by the National Institutes of Health. I suppose this is due to my experience with many aspects of the NIH grant process, from applying for grants, reviewing other applicant's grants and trying to get by at LANL using NIH money. However, there are many other investigators in B Division and elsewhere in LANL with similar or greater experience, so I am going to approach this from an interactive type of information service and solicit input from other NIH experts as well as from the general B Division investigator community. Topics that I have planned to address in the next few issues include

- resources for learning about NIH grant solicitations
- putting together an NIH application budget
- what happens to your grant after submission
- LANL taxation of NIH grant money
- coordination of responses to NIH solicitations
- special awards and program project grants
- other resources of NIH information within and without B Division
- the role of a LANL NIH program office

The due date for regular NIH applications will be about 2 weeks after this issue of B Scene appears, so presumably those people preparing grants for this round are already well along toward having a finished product to submit. Accordingly, I will start out this column in the next issue discussing the first topic above: resources for learning about NIH solicitations. I will then follow along in subsequent columns in a somewhat organized approach to preparing and submitting an NIH proposal for the next funding round, which has a due date of June 1, 2000. Recognizing that having almost 20 years of experience with the NIH system can be a problem in my choice of topics, I would like to also address issues that are raised by the B Division community. I am also soliciting questions or suggestions for topics for this column in the future."

➤ *Contact: Jim Freyer (freyer@lanl.gov)*

Maryann Martinez reports that a web site has been established to help guide investigators through the NIH proposal preparation process. Look for it at:

http://telomere.lanl.gov/b_internal/NIH_help/

Bravo

New NIH Award

Mark MacInnes reports activation this week of a new 3-year NIH RO-1 grant: 'Ape/Ref Transgenes'. So, you ask, what's that?? The base repair enzyme Apurinic endonuclease is a multifunctional protein - both an endonuclease and also a cysteine oxidoreductase capable of reducing many key transcription factors *in vitro* and *in vivo*. The protein is known by many names including APE, APEX, REF-1, and HAP-1. "We call it Ape/Ref." MacInnes is now funded by NIGMS to study the redox

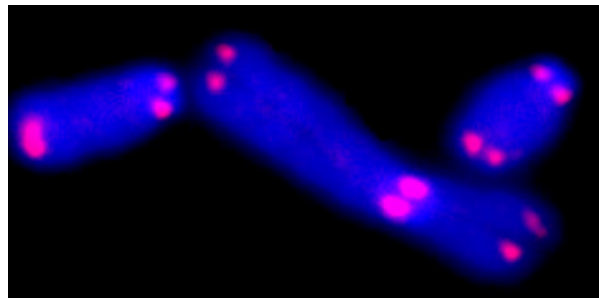
functions of this protein, in particular, hypothetical redox regulation of base damage repair. He will study mouse transgenic and cellular expression of mutant Ape/Ref proteins under oxidative and damaging cell stresses (acute and LLIR, pro-oxidant chemicals and hypoxia). The hypothesis he is testing is whether the Ape/Ref redox domain (in the unique n-terminal 100 AA) is important for affecting the level of base damage DNA repair in cells and tissues in vivo. Two ways this could occur are by increased nuclear localization / stabilization of Ape/Ref via association with key transcription factors, or alternatively, by autoregulation of Ape/Ref gene expression by its redox mechanism. Ape/Ref is translocated to the nucleus after certain cell stresses. An inter-molecular association is known to occur with thioredoxin in the redox domain. Thioredoxin is also translocated to the nucleus by cell stresses and cell proliferation stimuli. "What we don't know is whether these translocations are coupled, and, whether this localization increases the level of cell nucleus DNA base repair?" The Ape/Ref gene is also inducible. The autoregulatory (redox controlled?) aspects of this induction are still speculative. Says MacInnes, "I look forward to further discussions and potential collaborations on this topic arising from the new B-Scene!"

➤ *Contact: Mark A. MacInnes, mc@lanl.gov*

Breaking News

DNA Double-Strand Break Repair Proteins Are Required to Cap the Ends of Mammalian Chromosomes

Recent findings intriguingly place DNA double-strand break (dsb) repair proteins at chromosome ends in yeast where they help maintain normal telomere length and structure. In the present study, an essential telomere function, the ability to cap and thereby protect chromosomes from end-to-end fusions, was assessed in repair-deficient mouse cell lines. Using fluorescence in situ hybridization (FISH) with a probe to telomeric DNA, spontaneously occurring chromosome aberrations were examined for telomere signal at the points of



Chromosome aberrations illustrating telomeric fusions

fusion, a clear indication of impaired end-capping. Telomeric fusions were not observed in any of the repair-proficient controls and occurred only rarely in a

p53 null mutant. In striking contrast, chromosomal end fusions that retained telomeric sequence were observed in non-transformed DNA-PKcs deficient cells where they were a major source of chromosomal instability. Metacentric chromosomes created by telomeric fusion became even more abundant in these cells following spontaneous immortalization. Restoration of repair proficiency through transfection with a functional cDNA copy of the human DNA-PKcs gene reduced the number of fusions compared to a negative transfection control. Virally transformed cells derived from Ku70 and Ku80 knockout mice also displayed end-to-end fusions. These studies demonstrate that DNA double-strand break repair genes play a dual role in maintaining chromosomal stability in mammalian cells; the known role in repairing incidental DNA damage, as well as a new protective role in telomeric end-capping. Abstract reprinted from PNAS, Dec 21, 1999, vol 96, no 26, 14899-14904. Authors: Susan M. Bailey, Julianne Meyne, David J. Chen, Akihiro, Kurimasa, Gloria C. Li, Bruce E. Lehnert and Edwin H. Goodwin. Stefan Burde assisted with the images.

➤ *Contributed by Susan Bailey (sbailey@lanl.gov).*

B There

B Division Calender and Events

The B Division staff seminar series has resumed on Mondays at 11 AM in the HRL auditorium. January 24, Andrew Bardbury, "Phages are Phun" January 31, Rich Okinaka, "Bacillus Anthracis: Virulence Plasmids and Phylogeny"

TECH TIME at HRL on Thursday 20 January at 11:00 A.M and in TA-35 conference room in Bldg. 2, Room B125 on February 2 at 11:00 A.M.

Sensor Workshop in Santa Fe, Feb. 28-29, 2000. The Sensor Technologies: Needs and Assessment Symposium, organized jointly by Los Alamos National Laboratory (LANL) and the Center for Process Analytical Chemistry (CPAC), University of Washington, Seattle, will be held Feb. 28-29, 2000, in Santa Fe, NM. Focus will be on the role of advances in measurement technology for applications in biotechnology, pharmaceuticals and food safety.

The objectives of the gathering are to identify and prioritize needs in technology development, identify barriers to marketplace deployment of pre-competitive technology, and explore potential industrial applications for detection technologies developed for national security. The meeting will consist of presentations and discussions. For more information, or register on-line through the web-sit:

http://www.lanl.gov/programs/bioscience/Sensor_ws/meeting_contacts.htm.

➤ *Contributed by Basil Swanson (basil@lanl.gov).*

B Happy!

The B Division Celebration held on December 1 drew smiles all around. *Photos by Liz Padilla, Public Affairs Office*



Bill Press (holding the key to B Division) and John Browne



Evelyn Campbell and Min Park.



Donna Gadbois



Hans Frauenfelder and Jill Trehwella



Scott Cram

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EDITOR
Babs Marrone

CONTRIBUTING EDITOR
Sandra Zink

Contact us at bscene@telomere.lanl.gov



Jian Song and Connie Campbell